REMARKS

I. Amendments

Claims 35 and 40 have been amended. Claims 36-37 and 42-46 have been canceled. Claims 11-16 and 29-34 have also been canceled, as they were withdrawn from consideration for being directed to non-elected subject matter. The amendment does not add or constitute new matter, and is completely supported by the application as originally filed. Support may be found throughout the specification and in the originally filed claims.

The amendments to and cancellation of claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in related applications. The amendment is not intended to limit the scope of the invention, and is made solely in order to put the claims in condition for allowance in response to the Final Office Action. The Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation or continuation-in-part application.

Upon entry of the amendment, claims 35 and 38-41 are pending in the instant application.

II. Rejections

A. Rejection under 35 U.S.C. § 112, first paragraph

Claims 35-46 were rejected under 35 U.S.C. § 112, first paragraph, because, according to the Examiner, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The Applicant respectfully disagrees, and traverses the rejection. However, in light of the amendments to the claims, the Examiner's rejection under 35 U.S.C. § 112, first paragraph, is no longer relevant, as noted below.

In the rejection, the Examiner asserts that the specification, while being enabling for a homozygous intestinal alkaline phosphatase gene knockout mouse that lacks production of functional intestinal alkaline phosphatase protein and exhibits the disclosed phenotype of abnormal activity level and a method of making said mouse, does not reasonably provide enablement for any type of intestinal alkaline phosphatase disruption exhibiting the phenotype of a nociceptive abnormality.

With regard to the type of disruption, the Applicant believes the specification sufficiently defines and describes the disruption in such a way as to enable one skilled in the art to create the transgenic mouse with the intestinal alkaline phosphatase disruption as claimed.

However, the Applicant has amended the claims in order to place them in condition for allowance, rendering the rejection moot.

With respect to the phenotype of a nociceptive abnormality, the Applicants reiterate their previous argument in response to this same rejection set forth in the Office Action mailed August 26, 2002 (see pages 5-6 of the response filed January 27, 2003). The Examiner has maintained her assertion that the specification presents hot plate data for only two pairs of mice, and that one pair of mice appears to have similar latencies. The Examiner further maintained that the phenotype appears inconsistent between the two pairs of wild-type and knockout mice. The Examiner also has alleged that it is unclear whether the hot plate test indicates thermal sensitivity, pain sensitivity and/or nociceptive sensitivity.

The Applicant respectfully disagrees and submits that the Examiner's conclusions remain inaccurate. Applicant again draws the Examiner's attention to the column labeled "count" under "Hot Plate" in Table 1 of the instant application. This column refers to the number of mice of each genotype and generation subjected to the Hot Plate test. Consequently, the Examiner's assertion that the specification provides data for only two pair of mice is incorrect. Further, Examiner's bald opinion that the latencies are "very similar" is both inappropriate and inaccurate. In fact, as shown by the data provided in Table 1, both the F2N0 and the F2N1 generations of knockout mice display a decreased latency to respond to a thermal stimulus, relative to wild-type mice of the same generation, with the F2N1 knockout mice showing a more marked decrease in response latency. Therefore, Applicant respectfully disagrees with the Examiner's assertion that the phenotype is inconsistent between the two pairs of wild-type and knockout mice. The Applicant further submits that one skilled in the art would be aware of the hot plate test, or similar procedures, and how to use them to assess sensitivity to a thermal stimulus or sensitivity to pain, without undue experimentation.

In any case, in order to place the claims in condition for allowance, the Applicant has amended claims 35 and 40 and canceled claims 36-37 in the instant amendment. As such, the rejections are no longer relevant, and Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 112, first paragraph. The Applicant submits that claims 35 and 38-41, in their current form, fully meet the requirements and are patentable under 35 U.S.C. § 112, first paragraph.

B. Rejection under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claim 40 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner rejects claim 40 in that the recitation of "breeding the chimeric mouse to produce the transgenic" renders the claim indefinite because it is unclear what is being produced, and has requested appropriate correction. The amendment to claim 40 incorporates the necessary correction, rendering the rejection moot.

The Applicant requests withdrawal of the rejection under 35 U.S.C. § 112, second paragraph. The Applicant submits that claims 35 and 38-41 are definite and particularly point out and distinctly claim the subject matter which applicant regards as the invention as required by the second paragraph of 35 U.S.C. § 112.

C. Rejection under 35 U.S.C. § 103

The Examiner has rejected claims 42-46 under 35 U.S.C. § 103 (a) as being unpatentable over Mansour *et al.*,1998, *Nature*, 336(24):348-352 ("Mansour") in view of Manes *et al.*, 1990, *Genomics.*, 8: 541-554 ("Manes"). The Applicant respectfully traverses the rejection. However, in order to place the claims in condition for allowance, the Applicant has canceled claims 42-46.

As the obviousness rejection is no longer relevant as a result of the cancellation of claims 42-46, the Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 103. Applicants believe pending claims 35 and 38-41 to be free of the prior art cited by the Examiner.

It is believed that the claims are now in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-173.

Respectfully submitted,

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